REMARKS

Claims 65-66, and 70-72 have been amended as set forth in the above complete listing of the claims. Claims 8-11, 14-61, and 69 are herein cancelled without prejudice or disclaimer. Thus, upon entry of the amendments, claims 62-68, and 70-72 will be pending.

Regarding the Amendments

The specification has been amended at page 14, lines 3-7, to clarify the use of trademarks in the specification. It is submitted that the amendment merely addresses a formality, and does not add new matter. Accordingly, entry of the amendment is respectfully requested.

Claims 8-11, 14-61, and 69 have been cancelled without prejudice or disclaimer.

Claims 65-66, and 70-72 have been amended to recite the term "isolated nucleic acid", thereby clarifying the subject matter regarded as the invention. As such, it is submitted that the amendments do not add new matter.

Claim 66 has been further amended to recite that the claimed isolated nucleic acid comprises "at least 40 bases in length" and is "identical to a contiguous portion of the sequence as set forth in SEQ ID NO: 26." The amendment is supported, for example, at page 12, lines 21-26. As such, it is submitted that this amendment to claim 66 does not add new matter.

Regarding the Restriction Requirement

Applicants acknowledge the election of Group XII, consisting of claims 62-72, and withdrawal of claims 8-11, and 14-61 from consideration by the Examiner as being drawn to non-elected inventions. However, in order to focus the claims on the elected group, claims 8-11, and 14-61 have been cancelled herein.

Regarding the Specification

The Examiner has noted the use of a trademarks throughout the application. It is noted in the Office Action mailed August 26, 2003 that the use of trademarks is allowed and such trademarks should be capitalized and accompanied by the generic terminology. Accordingly, Applicants have requested amendment of various paragraphs of the specification, as set forth above in the "amendments" section. These amendments do not add any new matter, but clarify the use of trademarks in the specification. All trademarks utilized are followed with the symbol ®, indicating a registered trademark and are in all capital letters.

Rejection Under 35 U.S.C. § 101

Applicants respectfully traverse the rejection of claims 62-72 under 35 U.S.C, §101 as allegedly lacking utility.

Applicants respectfully submit that the specification provides ample support for specific, substantial and credible utility of the present invention. For example, Applicants' invention provides nucleic acid and polypeptide sequences of novel immediate early genes whose expression is rapidly increased immediately following stimulation. Expression of invention nucleic acids and polypeptides is induced by brain activation (specification, page 41, lines 7-9) including, for example, by maximal electroconvulsive seizure (MECS). Since expression of invention nucleic acids and polypeptides in certain tissues, *e.g.*, cardiac and neuronal tissues, is specifically and rapidly altered in response to specialized activation, expression of these nucleic acids and polypeptides is a useful marker of identified, physiologically significant events.

MECS stimulation is a model for acute seizures and kainate- and PTZ-induced seizures are models for epilepsy (*see* Löscher and Schmidt, *Epilepsy Res.* 2:145-181 (1988), a copy of which is provided herewith as Exhibit A). Induction of gene expression in response to MECS (SEQ ID NO: 12, 18, 19, 26, 31, 46, 58), kainate-treatment (SEQ ID NO: 19, 26, 31) or PTZ-treatment (SEQ ID: 26, 31, 58) demonstrates that the up-regulated nucleic acids are indicator molecules for seizures. The nucleic acid described by SEQ ID NO: 26 is highly upregulated in

all three independent models. The relative level of gene expression of these indicator molecules can be used for determining both the occurrence and the severity of acute seizures.

Epileptic seizure and ischemia can be identified by the expression of invention nucleic acids and polypeptides in response to such events. Seizure and ischemia result in a reproducible and specific pattern of expression in brain and other tissues. For example, invention nucleic acid sequence, L100 (SEQ ID NO: 26), is weakly expressed in wild-type rat brain. Following seizure, however, expression is increased 17.2 fold in the hippocampus, dentate gyrus, entorrhinal cortex, the cingulum and fimbria (Specification, page 68, line 22 to page 71, line 20). In contrast, expression of L100 is unchanged in response to ischemia.

In summary, the specification provides ample support including numerous examples that demonstrate rapid expression of invention nucleic acid sequences and polypeptides in the brain and other tissues in response to stimulation or ischemia. Expression is indicative of the physiological event and thus, expression of invention nucleic acids and polypeptide can be a specific marker for seizure and ischemia. Accordingly, Applicants respectfully submit that the present invention provides a fully disclosed specific, substantial and credible utility and respectfully request reconsideration and withdrawal of the rejection of claims 1 to 7, 12 and 13 under 35 U.S.C § 101.

Rejections Under 35 U.S.C. § 112

The rejection of claims 62-72 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement in conjunction with the above utility rejection, is respectfully traversed.

Applicants submit that the claimed invention is adequately enabled by the specification because the invention does possess patentable utility, as set forth above. Expression of nucleic acids of the invention is induced by brain activation (specification, page 41, lines 7-9) including, for example, by maximal electroconvulsive seizure (MECS). Since expression of invention nucleic acids and polypeptides in certain tissues, such as cardiac and neuronal tissues, is specifically and rapidly altered in response to specialized activation, expression of these nucleic acids and polypeptides is a useful marker of identified, physiologically significant events. As

such, it is submitted that a person of ordinary skill in the art, viewing the specification, would be able to discern, without undue experimentation, how to use the claimed nucleic acids as specific markers for seizure and ischemia. Accordingly, withdrawal of the rejection of claims 62-72 under 35 U.S.C. § 112, first paragraph is respectfully requested.

Applicants respectfully traverse the rejection of claims 62-64 and 66-71 under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description. It is initially noted that claim 69 has been cancelled and claim 66 has been amended.

It is acknowledged in the Office Action that the specification adequately describes a nucleic acid molecule which encodes a protein having the amino acid sequence of SEQ ID NO: 27, including the nucleic acid as set forth in SEQ ID NO: 26. It is alleged, however, that the specification does not describe any other nucleic acid sequences which lack the sequence of SEQ ID NO: 26, and, therefore, does not support those isolated nucleic acids that are at least 60% or 85% identical to SEQ ID NO: 26 or to nucleic acids that encode proteins which have at least 60% identity to SEQ ID NO: 27 or to fragments of at least 12 bases of SEQ ID NO: 26 or at least 5 amino acids of SEQ ID NO: 27.

Applicants submit, however, that the disclosure in the specification is sufficient to apprise one skilled in the art that applicants were in possession of the claimed nucleic acids because 1) particular sequences (SEQ ID NO: 26, SEQ ID NO: 27) are disclosed; 2) the specification explicitly provides that nucleic acids of the invention include nucleic acids that are at least 60% or 85% identical to SEQ ID NO: 26 (see, for example, page 11, line 7-13), or that encode proteins which have at least 60% identity to SEQ ID NO: 27 (see, for example, page 11, line 27 to page 12, line 2), or to fragments of at least 40 bases of SEQ ID NO: 26 (see, for example, page 12, lines 21-26); and 3) the specification provides a detailed description of how to identify such nucleic acids.

The disclosure, as filed, recites full-length nucleic acid sequences of SEQ ID NO: 26 which can increase expression upon seizure induction and can influence neuronal activities involved in brain functions (Specification, page 8, lines 2-13). The specification further provides

that an isolated nucleic acid having 60 percent or 85 percent identity to the sequence as set forth in SEQ ID NO: 26 (page 11, lines 11-13) are within the scope of the invention. Similarly, a full-length amino acid sequence of SEQ ID NO: 27 is disclosed, along with nucleic acids that encode amino acids with at least 60 percent identity to SEQ ID NO: 27 (see, for example, page 11, line 27, to page 12, line 4). The specification provides a detailed description of a method to determine percent identity between related sequences (see, for example, page 11, lines 12-24, and page 12, lines 4-16). For example, the specification provides that sequence alignment software is used to compare positions between two sequences and, using the Jotun Heim algorithm, percent identity can be calculated. Thus, those of skill in the art, viewing the specification, would recognize that Applicants were in possession of sequences with 60 or 85 percent identity to the particular sequences listed in the specification (SEQ ID NO: 26, SEQ ID NO: 27).

Applicants therefore submit that it is not necessary that the specification individually list each and every nucleic acid sequence having 60 or 85 percent identity to the listed sequences, or each fragment of SEQ ID NO: 26, because, in light of the guidance provided in the specification, identification of such sequences would have been routine and within the ordinary skill of those in the art. The Examiner's attention is respectfully drawn to the MPEP § 2163 II.A.3.(a), which provides the following:

> "what is conventional or well known to one of ordinary skill in the art need not be disclosed in detail...If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met."

Thus, for the reasons set forth above, the specification provides adequate disclosure and guidance, such that one skilled in the art would have recognized that Applicants were in possession of the claimed nucleic acids.

Accordingly, it is submitted that claims 62-64 and 66-71 meet the written description requirement of 35 U.S.C. §112, first paragraph, and removal of the rejection is respectfully requested.

Applicants respectfully traverse the rejection of claims 65, 66 and 69-72 under 35 U.S.C. §112, second paragraph as allegedly indefinite for failing to point out and distinctly claim the subject matter of the invention. In particular, it is alleged that the use of the term "sequence" is not allowed in the claims and that the term "isolated nucleic acid" should be utilized instead.

Claims 65-66, and 70-72 have been amended in accordance with the Examiner's suggestion, thereby clarifying the subject matter regarded as the invention. Claim 69 has been cancelled. Accordingly, removal of this ground of rejection is respectfully requested.

Additionally, Applicants respectfully traverse the rejection of claim 66 under 35 U.S.C. §112, second paragraph as allegedly indefinite, for recitation of hybridization "under moderately stringent or highly stringent hybridization conditions."

It is alleged that the metes and bounds of the claimed invention cannot be defined because a precise set of hybridization conditions are not disclosed in the claims or the specification. However, Applicants submit that conditions for hybridization under moderately or highly stringent conditions are clearly set forth in the specification. The Examiner's attention is respectfully drawn to the specification, at page 12, lines 1-10, which specifically sets forth the elements of high and moderate stringency hybridization conditions. Accordingly, it is respectfully submitted that, as the claims of the invention read in light of the specification, one of skill in the art would be able to practice the invention without the inclusion of the specific hybridization conditions in claim 66.

Therefore, Applicants submit that claims 65, 66 and 69-72 meet the definiteness requirement of 35 U.S.C. §112, second paragraph, and the removal of the rejection is respectfully requested.

Rejection Under 35 U.S.C. § 102

Applicants respectfully traverse the rejection of claim 66 under 35 U.S.C. 102(b) as allegedly anticipated by Marra et al.

It is stated in the Office Action that Marra et al disclose a sequence that comprises at least 12 bases identical to those disclosed in SEQ ID NO: 26 of the instant invention. In order to advance the prosecution of the present application, claim 66 has been amended to more clearly define the claimed subject matter. Accordingly, removal of the rejection of claim 66 under 35 U.S.C. 102(b) is respectfully requested.

Applicants respectfully traverse the rejection of claim 69 under 35 U.S.C. 102(b) as allegedly anticipated by Andrae et al.

In particular, it is stated in the Office Action that Andrae et al teaches a polypeptide which meets the description of the "claimed fragment" of claim 69. Applicants note, however, that claim 69 is directed to an isolated nucleic acid, not a polypeptide fragment, and the polypeptide of the cited reference does not teach each and every element of the claimed nucleic acid. Nevertheless, Applicants point out that claim 69 has been cancelled, thereby rendering the rejection moot. Accordingly, Applicants respectfully request removal of the rejection of claim 69 under 35 U.S.C. 102(b).

CONCLUSION

In summary, for the reasons set forth herein, Applicants maintain that claims 62-68, and 70-72 clearly and patentably define the invention, respectfully request that the Examiner reconsider the various grounds set forth in the Office Action, and respectfully request the allowance of the claims which are now pending.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative can be reached at (858) 677-1456. Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

Date: January 23, 2004

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Enclosure: Exhibit A